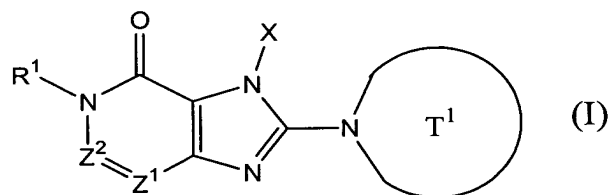


**Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

1. (Original) A pharmaceutical agent comprising a dipeptidyl peptidase IV inhibitor and a biguanide agent in combination.
2. (Original) The pharmaceutical agent according to claim 1, which enhances the effects of active circulating glucagon-like peptide-1 (GLP-1) and/or active circulating glucagon-like peptide-2 (GLP-2).
3. (Original) A pharmaceutical agent that enhances the effects of active circulating GLP-2.
4. (Original) A pharmaceutical agent comprising a dipeptidyl peptidase IV inhibitor and the pharmaceutical agent according to claim 3 in combination.
5. (Original) The pharmaceutical agent according to claim 1 or 4, wherein the dipeptidyl peptidase IV inhibitor is a compound represented by the following formula, or a salt or hydrate thereof,



(wherein,

T<sup>1</sup> represents a monocyclic or bicyclic 4- to 12-membered heterocyclic group containing one or two nitrogen atoms in the ring, that may have one or more substituents;

X represents a C<sub>1-6</sub> alkyl group which may have one or more substituents, a C<sub>2-6</sub> alkenyl group which may have one or more substituents, a C<sub>2-6</sub> alkynyl group which may have one or more substituents, a C<sub>6-10</sub> aryl group which may have one or more

substituents, a 5 to 10-membered heteroaryl group which may have one or more substituents, a C<sub>6-10</sub> aryl C<sub>1-6</sub> alkyl group which may have one or more substituents, or a 5 to 10-membered heteroaryl C<sub>1-6</sub> alkyl group which may have one or more substituents;

Z<sup>1</sup> and Z<sup>2</sup> each independently represent a nitrogen atom or a group represented by the formula -CR<sup>2</sup>=;

R<sup>1</sup> and R<sup>2</sup> each independently represent a group according to the formula -A<sup>0</sup>-A<sup>1</sup>-A<sup>2</sup> (wherein

A<sup>0</sup> represents a single bond or a C<sub>1-6</sub> alkylene group, which may have 1 to 3 substituents selected from group B consisting of the substituents described below;

A<sup>1</sup> represents a single bond, an oxygen atom, a sulfur atom, a sulfinyl group, a sulfonyl group, a carbonyl group, a group represented by the formula -O-CO-, a group represented by the formula -CO-O-, a group represented by the formula -NR<sup>A</sup>-, a group represented by the formula -CO-NR<sup>A</sup>-, a group represented by the formula -NR<sup>A</sup>-CO-, a group represented by the formula -SO<sub>2</sub>-NR<sup>A</sup>-, or a group represented by the formula -NR<sup>A</sup>-SO<sub>2</sub>-;

A<sup>2</sup> and R<sup>A</sup> each independently represent a hydrogen atom, a halogen atom, a cyano group, a C<sub>1-6</sub> alkyl group, a C<sub>3-8</sub> cycloalkyl group, a C<sub>2-6</sub> alkenyl group, a C<sub>2-6</sub> alkynyl group, C<sub>6-10</sub> aryl group, a 5 to 10-membered heteroaryl group, a 4 to 8-membered heterocyclic group, a 5 to 10-membered heteroaryl C<sub>1-6</sub> alkyl group, a C<sub>6-10</sub> aryl C<sub>1-6</sub> alkyl group, or a C<sub>2-7</sub> alkylcarbonyl group;

however, A<sup>2</sup> and R<sup>A</sup> each independently may have 1 to 3 substituents selected from the substituent group B described below:

when Z<sup>2</sup> is a group represented by the formula -CR<sup>2</sup>=, R<sup>1</sup>, and R<sup>2</sup> may in combination form a 5 to 7-membered ring;

except in cases where: [1] R<sup>1</sup> is a hydrogen atom; Z<sup>1</sup> is a nitrogen atom; and Z<sup>2</sup> is -CH=; and [2] Z<sup>1</sup> is a nitrogen atom; and Z<sup>2</sup> is -C(OH)=;

<Substituent group B>

Substituent group B represents the group consisting of: a hydroxyl group, a mercapto group, a cyano group, a nitro group, a halogen atom, a trifluoromethyl group, a C<sub>1-6</sub> alkyl group which may have one or more substituents, a C<sub>3-8</sub> cycloalkyl group, a C<sub>2-6</sub> alkenyl group, a C<sub>2-6</sub> alkynyl group, a C<sub>6-10</sub> aryl group, a 5 to 10-membered heteroaryl group, a 4 to 8-membered heterocyclic group, a C<sub>1-6</sub> alkoxy group, a C<sub>1-6</sub> alkylthio group, a group represented by the formula -SO<sub>2</sub>-NR<sup>B1</sup>-R<sup>B2</sup>, a group represented by the formula -NR<sup>B1</sup>-CO-R<sup>B2</sup>, a group represented by the formula -NR<sup>B1</sup>-R<sup>B2</sup> (where R<sup>B1</sup> and R<sup>B2</sup> each independently represent a hydrogen atom or a C<sub>1-6</sub> alkyl group), a group represented by the formula -CO-R<sup>B3</sup> (where R<sup>B3</sup> represents a 4 to 8-membered heterocyclic group), a group represented by the formula -CO-R<sup>B4</sup>-R<sup>B5</sup> and a group represented by the formula -CH<sub>2</sub>-CO-R<sup>B4</sup>-R<sup>B5</sup> (where R<sup>B4</sup> represents a single bond, an oxygen atom, or a group represented by the formula -NR<sup>B6</sup>-; R<sup>B5</sup> and R<sup>B6</sup> each independently represent a hydrogen atom, a C<sub>1-6</sub> alkyl group, a C<sub>3-8</sub> cycloalkyl group, a C<sub>2-6</sub> alkenyl group, a C<sub>2-6</sub> alkynyl group, a C<sub>6-10</sub> aryl group, a 5 to 10-membered heteroaryl group, a 4 to 8-membered heterocyclic C<sub>1-6</sub> alkyl group, a C<sub>6-10</sub> aryl C<sub>16</sub> alkyl group, or a 5 to 10-membered heteroaryl C<sub>1-6</sub> alkyl group)).

6. (Original) The pharmaceutical agent according to claim 5, wherein T<sup>1</sup> is a piperazin-1-yl group or a 3-amino-piperidin-1-yl group.

7. (Original) The pharmaceutical agent according to claim 5, wherein T<sup>1</sup> is a piperazin-1-yl group.

8. (Currently Amended) The pharmaceutical agent according to claim 5 ~~any one of claims 5 to 7~~, wherein X is a 3-methyl-2-buten-1-yl group, a 2-butyryl group, a benzyl group, or a 2-chlorophenyl group.

9. (Currently Amended) The pharmaceutical agent according to claim 5 ~~any one of claims 5 to 7~~, wherein X is a 2-butynyl group.

10. (Currently Amended) The pharmaceutical agent according to claim 5 ~~any one of claims 5 to 9~~, wherein,

$Z^1$  is a nitrogen atom; and

$Z^2$  is a group represented by the formula  $-CR_2=$

(where  $R^2$  is as defined in claim 5).

11. (Currently Amended) The pharmaceutical agent according to claim 5 ~~any one of claims 5 to 9~~, wherein,

$Z^2$  is a nitrogen atom; and

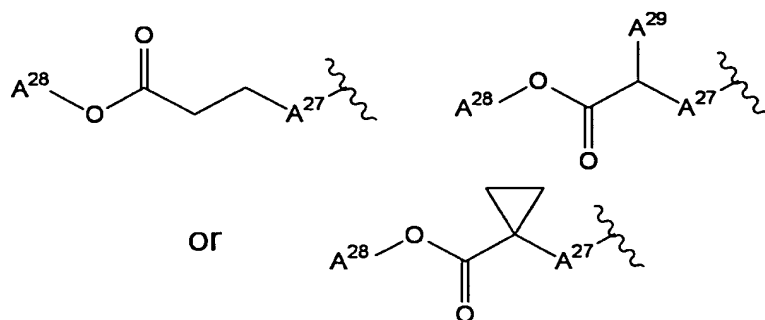
$Z^1$  is a group represented by the formula  $-CR_2=$

(where  $R^2$  is as defined in claim 5).

12. (Currently Amended) The pharmaceutical agent according to claim 5 ~~any one of claims 5 to 11~~, wherein  $R^1$  is either a methyl group, a cyanobenzyl group, a fluorocyanobenzyl group, a phenethyl group, a 2-methoxyethyl group, or a 4-methoxycarbonylpyridin-2-yl group.

13. (Currently Amended) The pharmaceutical agent according to claim 5 ~~any one of claims 5 to 11~~, wherein  $R^1$  is a methyl group, or a 2-cyanobenzyl group.

14. (Currently Amended) The pharmaceutical agent according to claim 5 ~~any one of claims 5 to 13~~, wherein  $R^2$  is either a hydrogen atom, a cyano group, a methoxy group, a carbamoylphenoxy group, or a group represented by the formula:



(where,

A<sup>27</sup> represents an oxygen atom, a sulfur atom, or -NH-;

A<sup>28</sup> and A<sup>29</sup> each independently represent a hydrogen atom or a C<sub>1-6</sub> alkyl group).

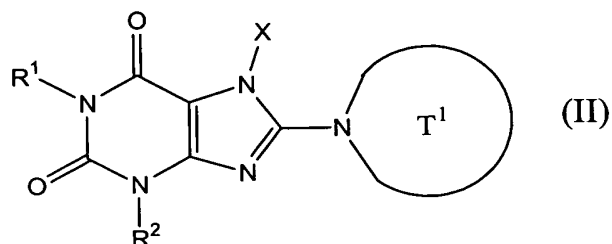
15. (Currently Amended) The pharmaceutical agent according to claim 5 ~~any one of claims 5 to 13~~, wherein R<sup>2</sup> is a hydrogen atom, a cyano group, or a 2-carbamoylphenyloxy group.

16. (Original) The pharmaceutical agent according to claim 5, wherein the compound represented by formula (I) is any one compound selected from:

- (1) 7-(2-butynyl)-2-cyano-1-methyl-8-(piperazin-1-yl)-1,7-dihydropurin-6-one;
- (2) 3-(2-butynyl)-5-methyl-2-(piperazin-1-yl)-3,5-dihydroimidazo[4,5-d]pyridazin-4-one;
- (3) 2-(3-aminopiperidin-1-yl)-3-(2-butynyl)-5-methyl-3,5-dihydroimidazo[4,5-d]pyridazin-4-one;
- (4) 2-[7-(2-butynyl)-1-methyl-6-oxo-8-(piperazin-1-yl)-6,7-dihydro-1H-purin-2-yloxy] benzamide;
- (5) 7-(2-butynyl)-1-(2-cyanobenzyl)-6-oxo-8-(piperazin-1-yl)-6,7-dihydro-1H-purine-2-carbonitrile; and
- (6) 2-[3-(2-butynyl)-4-oxo-2-(piperazin-1-yl)-3,4-dihydroimidazo[4,5-d]pyridazin-5-ylmethyl] benzonitrile;

or a salt or hydrate thereof.

17. (Currently Amended) The pharmaceutical agent according to claim 1 or 4, wherein the dipeptidyl peptidase IV inhibitor is a compound represented by the following formula, or a salt or hydrate thereof,



(wherein  $T^1$ ,  $X$ ,  $R^1$ , and  $R^2$  are as defined in claim 5)

$T^1$  represents a monocyclic or bicyclic 4- to 12-membered heterocyclic group containing one or two nitrogen atoms in the ring, that may have one or more substituents;

$X$  represents a  $C_{1-6}$  alkyl group which may have one or more substituents, a  $C_{2-6}$  alkenyl group which may have one or more substituents, a  $C_{2-6}$  alkynyl group which may have one or more substituents, a  $C_{6-10}$  aryl group which may have one or more substituents, a 5 to 10-membered heteroaryl group which may have one or more substituents, a  $C_{6-10}$  aryl  $C_{1-6}$  alkyl group which may have one or more substituents, or a 5 to 10-membered heteroaryl  $C_{1-6}$  alkyl group which may have one or more substituents;

$R^1$  and  $R^2$  each independently represent a group according to the formula  $-A^0-A^1-A^2$

(wherein

$A^0$  represents a single bond or a  $C_{1-6}$  alkylene group, which may have 1 to 3 substituents selected from group B consisting of the substituents described below;

$A^1$  represents a single bond, an oxygen atom, a sulfur atom, a sulfinyl group, a sulfonyl group, a carbonyl group, a group represented by the formula  $-O-CO-$ , a group represented by the formula  $-CO-O-$ , a group represented by the formula  $-NR^A-$ , a group represented by the formula  $-CO-NR^A-$ , a group represented by the formula  $-NR^A-CO-$ , a group represented by the formula  $-SO_2-NR^A-$ , or a group represented by the formula  $-NR^A-SO_2-$ ;

A<sup>2</sup> and R<sup>A</sup> each independently represent a hydrogen atom, a halogen atom, a cyano group, a C<sub>1-6</sub> alkyl group, a C<sub>3-8</sub> cycloalkyl group, a C<sub>2-6</sub> alkenyl group, a C<sub>2-6</sub> alkynyl group, C<sub>6-10</sub> aryl group, a 5 to 10-membered heteroaryl group, a 4 to 8-membered heterocyclic group, a 5 to 10-membered heteroaryl C<sub>1-6</sub> alkyl group, a C<sub>6-10</sub> aryl C<sub>1-6</sub> alkyl group, or a C<sub>2-7</sub> alkylcarbonyl group;

however, A<sup>2</sup> and R<sup>A</sup> each independently may have 1 to 3 substituents selected from the substituent group B described below:

<Substituent group B>

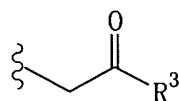
Substituent group B represents the group consisting of: a hydroxyl group, a mercapto group, a cyano group, a nitro group, a halogen atom, a trifluoromethyl group, a C<sub>1-6</sub> alkyl group which may have one or more substituents, a C<sub>3-8</sub> cycloalkyl group, a C<sub>2-6</sub> alkenyl group, a C<sub>2-6</sub> alkynyl group, a C<sub>6-10</sub> aryl group, a 5 to 10-membered heteroaryl group, a 4 to 8-membered heterocyclic group, a C<sub>1-6</sub> alkoxy group, a C<sub>1-6</sub> alkylthio group, a group represented by the formula -SO<sub>2</sub>-NR<sup>B1</sup>-R<sup>B2</sup>, a group represented by the formula -NR<sup>B1</sup>-CO-R<sup>B2</sup>, a group represented by the formula -NR<sup>B1</sup>-R<sup>B2</sup> (where R<sup>B1</sup> and R<sup>B2</sup> each independently represent a hydrogen atom or a C<sub>1-6</sub> alkyl group), a group represented by the formula -CO-R<sup>B3</sup> (where R<sup>B3</sup> represents a 4 to 8-membered heterocyclic group), a group represented by the formula -CO-R<sup>B4</sup>-R<sup>B5</sup> and a group represented by the formula -CH<sub>2</sub>-CO-R<sup>B4</sup>-R<sup>B5</sup> (where R<sup>B4</sup> represents a single bond, an oxygen atom, or a group represented by the formula -NR<sup>B6</sup>-; R<sup>B5</sup> and R<sup>B6</sup> each independently represent a hydrogen atom, a C<sub>1-6</sub> alkyl group, a C<sub>3-8</sub> cycloalkyl group, a C<sub>2-6</sub> alkenyl group, a C<sub>2-6</sub> alkynyl group, a C<sub>6-10</sub> aryl group, a 5 to 10-membered heteroaryl group, a 4 to 8-membered heterocyclic C<sub>1-6</sub> alkyl group, a C<sub>6-10</sub> aryl C<sub>1-6</sub> alkyl group, or a 5 to 10-membered heteroaryl C<sub>1-6</sub> alkyl group)).

18. (Original) The pharmaceutical agent according to claim 17, wherein T<sup>1</sup> is a piperazin-1-yl group.

19. (Currently Amended) The pharmaceutical agent according to claim 17-~~or~~ 18, wherein X is a 2-butynyl group or a 2-chlorophenyl group.

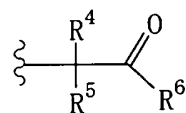
20. (Currently Amended) The pharmaceutical agent according to claim 17-~~or~~ 18, wherein X is a 2-butynyl group.

21. (Currently Amended) The pharmaceutical agent according to claim 17-~~any one of claims 17 to 20~~, wherein R<sup>1</sup> is a hydrogen atom, a methyl group, a 2-propynyl group, a 2-butynyl group, a cyanomethyl group, a phenethyl group, a phenoxyethyl group, or a group represented by the formula:



(where R<sup>3</sup> represents a hydroxyl group, a C<sub>1-6</sub> alkoxy group, or a phenyl group).

22. (Currently Amended) The pharmaceutical agent according to claim 17-~~any one of claims 17 to 21~~, wherein R<sup>2</sup> is a hydrogen atom, a C<sub>1-6</sub> alkyl group, an ethoxyethyl group, a tetrahydrofuranylmethyl group, or a group represented by the formula:

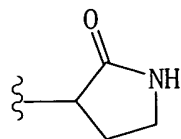


(where,

R<sup>4</sup> and R<sup>5</sup> are identical to or different from each other, and independently represent a hydrogen atom, a methyl group, or a phenyl group; and

R<sup>6</sup> represents a hydroxyl group, a C<sub>1-6</sub> alkoxy group, or a phenyl group),

or a group represented by the formula:



23. (Original) The pharmaceutical agent according to claim 17, wherein the



compound represented by formula (II) is any one compound selected from:

- (1) 7-(2-butynyl)-1,3-dimethyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
- (2) 7-(2-butynyl)-3-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
- (3) methyl [7-(2-butynyl)-3-methyl-2,6-dioxo-8-(piperazin-1-yl)-2,3,6,7-tetrahydropurin-1-yl] acetate;
- (4) 7-(2-butynyl)-3-methyl-8-(piperazin-1-yl)-1-(2-propynyl)-3,7-dihydropurine-2,6-dione;
- (5) 1,7-bis(2-butynyl)-3-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
- (6) [7-(2-butynyl)-3-methyl-2,6-dioxo-8-(piperazin-1-yl)-2,3,6,7-tetrahydropurin-1-yl] acetonitrile;
- (7) 7-(2-butynyl)-3-methyl-1-[(2-oxo-2-phenyl)ethyl]-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
- (8) 7-(2-butynyl)-3-ethyl-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
- (9) methyl [7-(2-butynyl)-1-methyl-2,6-dioxo-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl] acetate;
- (10) 7-(2-butynyl)-3-(2-tetrahydrofuranyl)methyl-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
- (11) methyl [7-(2-butynyl)-1-methyl-2,6-dioxo-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl]phenylacetate;
- (12) 7-(2-butynyl)-3-propyl-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
- (13) 7-(2-butynyl)-3-(2-oxo-2-phenethyl)-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
- (14) ethyl 2-[7-(2-butynyl)-1-methyl-2,6-dioxo-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl] propionate;
- (15) 7-(2-butynyl)-3-(2-ethoxyethyl)-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
- (16) 7-(2-butynyl)-3-isopropyl-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
- (17) 7-(2-butynyl)-3-(3,3-dimethyl-2-oxobutyl)-1-methyl-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;

- (18) 7-(2-butynyl)-1-methyl-3-(2-oxopyrrolidin-3-yl)-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
  - (19) 7-(2-butynyl)-3-(2-ethoxyethyl)-1-(2-oxo-2-phenylethyl)-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
  - (20) methyl [7-(2-butynyl)-2,6-dioxo-1-(2-oxo-2-phenylethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl] acetate;
  - (21) ethyl [7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl] acetate;
  - (22) [7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl] acetate;
  - (23) 7-(2-butynyl)-3-[2-oxo-2-(pyrrolidin-1-yl)ethyl]-1-(2-phenethyl)-8-(piperazin-1-yl)-3,7-dihydropurine-2,6-dione;
  - (24) 2-[7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl]-N-methylacetamide;
  - (25) 2-[7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl]-N-cyclopropyl acetamide;
  - (26) 2-[7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl]-N-phenylacetamide; and
  - (27) 2-[7-(2-butynyl)-2,6-dioxo-1-(2-phenethyl)-8-(piperazin-1-yl)-1,2,6,7-tetrahydropurin-3-yl]-N-(2-propynyl) acetamide;
- or a salt or hydrate thereof.

24. (Original) The pharmaceutical agent according to claim 1, wherein the biguanide agent is metformin.

25. (Original) The pharmaceutical agent according to claim 1 or 2, which is a preventive or therapeutic agent for a disease which is associated with active circulating GLP-1 and/or active circulating GLP-2.

26. (Original) The pharmaceutical agent according to claim 25, wherein the disease is at least any one selected from the group consisting of: diabetes, obesity, hyperlipidemia, and gastrointestinal diseases.

27. (Original) The pharmaceutical agent according to claim 3 or 4, which is a preventive or therapeutic agent for a disease which is associated with active circulating GLP-2.

28. (Original) The pharmaceutical agent according to claim 27, wherein the disease is a gastrointestinal disease.

29. (Original) A method for preventing or treating a disease which is associated with active circulating GLP-1 and/or active circulating GLP-2, which comprises administering the pharmaceutical agent according to claim 1 or 2 at an effective amount.

30. (Original) The use of the pharmaceutical agent according to claim 1 or 2 for producing a preventive or therapeutic agent for a disease which is associated with active circulating GLP-1 and/or active circulating GLP-2.

31. (Original) A method for preventing or treating a disease which is associated with active circulating GLP-2, which comprises administering the pharmaceutical agent according to claim 3 or 4 at an effective amount.

32. (Original) The use of the pharmaceutical agent according to claim 3 or 4 for producing a preventive or therapeutic agent for a disease which is associated with active circulating GLP-2.

33. (Original) A method for enhancing the effects of active circulating GLP-1 and/or active circulating GLP-2, which comprises using the pharmaceutical agent according to claim 1 or 2.

34. (Original) A method for enhancing the effects of active circulating GLP-2, which comprises using the pharmaceutical agent according to claim 3 or 4.